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Case Report
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Adoration of the Magi: Agammaglobulinemia of the Mother, Clinically Expressed in her Child

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Abstract

A newborn child, who suffered from two episodes of bacterial meningitis, was found to have an absence of IgG. Loss of IgG *via* kidneys or intestines was excluded. Next the mother was investigated who turned out to be agammaglobulinemic. IgG levels were below 1 g/L while IgM and IgA were normal. Mother was subsequently treated with gammaglobulin substitution therapy. The child produces normal levels of IgG and has remained infection free.

Clinical Case

A three week old boy, child of healthy, unrelated parents was admitted to the hospital because of bacterial meningitis. The pregnancy had been complicated by gestational diabetes, but the delivery after 38 weeks of pregnancy was uncomplicated. The child had normal length and weight for his gestational age and had a good start. The bacterial meningitis was treated with appropriate antibiotics and the child recovered completely within 5 days and was discharged. However, within two months, the child suffered from a second episode of bacterial meningitis, which was again treated successfully. Retrospective analysis of the infant's blood, taken at three weeks of age (during the first meningitis episode), showed an absence of IgG (<1.2 g/L; not quantitated with more sensitive methods), while IgM (1.3 g/L) and IgA (0.4 g/L) both were detectable. There were no indications for loss of IgG (nephrotic syndrome, protein losing enteropathy). The initial immune status investigations thus were focused on the child, and revealed (IgG) agammaglobulinemia. This was an unexpected finding, because at that age maternal IgG should still be present [1,2]. One reason for this finding might be a defect in transplacental transport of IgG from mother to child, which could be explained by a deficiency in the expression or function of the neonatal Fc-receptor (FcRn) [3,4]. Another explanation could be that the mother is agammaglobulinemic herself [5]. Therefore, the mother was evaluated.

The Adoration of the Magi is a popular theme in Christian art, mainly paintings but also sculpture and music. Figure 1 shows a fragment of the painting by Jheronimus Bosch, the master of the Northern renaissance. From the staging (mise-en-scene) it is clear that all the attention of the magi (only two out of the three are included in the fragment) is focused on the newborn child. Apart from the magi, who could be regarded as pediatricians, it is clear that there are other spectators, including shepherds, peasants and medical immunologists, all transfixed by the child.

In this clinical case there were, as indicated above, reasons to investigate the mother. The mother reported a relatively uncomplicated medical history. She did not smoke, had no known allergies, used no medications and did not report any symptoms or complaints at the time of evaluation. She reported having one episode of tonsillitis per year since more than ten years. She worked as an elementary school teacher.

Physical examination showed a healthy female, and no abnormalities were found. Specifically, there was no lymphadenopathy or splenomegaly and her palatine tonsils were relatively large but otherwise unremarkable. Laboratory analysis revealed severe hypogammaglobulinemia: Serum IgG was 0.57 g/L, IgM 0.4 g/L, and IgA 3.8 g/L. All IgG subclass levels were low/absent (Table 1). Circulating antibodies against specific antigens including diphtheria-tetanus-pertussis-poliomyelitis were, despite a normal vaccination history, undetectable. Blood B- lymphocytes and B lymphocyte

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Figure 1: Fragment of Jheronimus Bosch' painting The Adoration of the Magi, dated between 1485 and 1500 (Museo del Prado, Madrid, Spain). The fragment shows Balthazar kneeling and Melchior standing behind him in adoration of the newborn Jesus and his mother Mary. (Wikimedia Commons: Jheroniumus Bosch, Paintings 2.1.9: The Adoration of the Magi.

Table 1: Serum and saliva immunoglobulin levels of mother.

Serum	Patient	Reference range
IgM	0.4*	0.4-2.5
IgG	0.57	8.0-17.0
IgG1	0.5	4.9-11.4
IgG2	0.1	1.5-6.4
IgG3	<0.1	0.2-1.1
IgG4	<0.1	0.1-1.4
IgA	3.8	0.5-3.7
IgA1	2.9	0.6-2.4
IgA2	0.37	0.1-1.6
Saliva		
IgA	>100**	>60

*Immunoglobulin concentrations expressed as g/L; **mg/L

subsets, as well as T lymphocytes were normal (data not shown). An HRCT-scan of the thorax showed no abnormalities.

It is unknown how long this patient had been hypogammaglobulinemic prior to diagnosis. There was no remarkable history of infections, except for a yearly episode of tonsillitis. It would have been expected that such a low IgG concentration would be associated with more frequent and more serious infections. Potentially, the normal IgM and even high IgA concentrations could have offered protection against (mucosal) infections. After having made the diagnosis of agammaglobulinemia, the patient was treated with gammaglobulin substitution therapy (to be reported separately) [6].

The index patient with two episodes of bacterial meningitis was the third child in this family. The two older children had an unremarkable clinical and infectious history. The third child had no severe infectious episodes since the two episodes of meningitis. The serum immunoglobulin levels of all three children were measured one year after diagnosis of their mother. IgG, IgM and IgA levels turned out to be normal. These data underscore the conclusion that the episodes of bacterial meningitis in the newborn child were due to an immunodeficiency of the mother and not of the child itself.

This case therefore shows that when an immunodeficiency is suspected in a newborn child, the focus of clinical and diagnostic attention should not always be exclusively directly at the patient in question, but that mother should also be investigated.

References

1. Agarwal S, Cunningham-Rundles C. Assessment and clinical interpretation of reduced IgG values. Ann Allergy Asthma Immunol. 2007;99(3):281-3.
2. Grindstaff JL, Brodie ED, Ketterson ED. Immune function across generations: integrating mechanism and evolutionary process in maternal antibody transmission. Proc Biol Sci. 2003;270(1531):2309-19.
3. Stapleton NM, Einarsdóttir HK, Stemerding AM, Vidarsson G. The multiple facets of FcRn in immunity. Immunol Rev. 2015;268(1):253-68.
4. Wilcox CR, Holder B, Jones CE. Factors affecting the fcrn-mediated transplacental transfer of antibodies and implications for vaccination in pregnancy. Front Immunol. 2017;8:1294.
5. Berglöf A, Turunen JJ, Gissberg O, Bestas B, Blomberg KEM, Smith CE. Agammaglobulinemia: Causative mutations and their implications for novel therapies. Expert Rev Clin Immunol. 2013;9(12):1205-21.
6. Hoffman TW, van Kessel DA, van Velzen-Blad H, Grutters JC, Rijkers GT. Antibody replacement therapy in primary antibody deficiencies and iatrogenic hypogammaglobulinemia. Expert Rev Clin Immunol. 2015;11(8):921-33.